20. (New) The DNA molecule of claim 17 consisting of nucleotides 111 to 1086 of SEQ ID NO:1.

21. (New) A DNA molecule comprising a nucleotide sequence complementary to at least 10 nucleotides of SEQ ID NO:1.

22. (New) The DNA molecule of claim 21 comprising a nucleotide sequence complementary to at least 10 nucleotides of nucleotides 111 to 1086 of SEQ ID NO:1.

23. (New) A DNA molecule consisting of a nucleotide sequence complementary to at least 10 nucleotides of SEQ ID NO:1.

24. (New) The DNA molecule of claim 23 consisting of a nucleotide sequence complementary to at least 10 nucleotides of nucleotides 111 to 1086 of SEQ ID NO:1.

REMARKS

Following entry of the foregoing amendments, claims 17 to 24 will be pending in the application. Claims 1 to 3 and 10 to 12 have been cancelled, and new claims 17 to 24 have been added.

Applicants respectfully request reconsideration of the rejections of record in view of the foregoing amendments and the following remarks.

I. Objections to the Specification

A. The specification has been objected to because the addition of GenBank accession numbers to the paragraph spanning pages 6 and 7 of the specification in an amendment filed August 21, 2001 allegedly introduced new matter. Without conceding the correctness of the assertion, and to advance prosecution, the GenBank accession numbers have been deleted from the paragraph in question. The objection has been obviated, and Applicants respectfully request withdrawal thereof.

B. The specification has been objected to because it contains hyperlinks and other forms of browser-executable code. The specification has been amended to delete all hyperlinks and other forms of browser-executable code. The objection has been obviated, and Applicants respectfully request withdrawal thereof.

C. The specification has been objected to because the brief description of Figure 6 allegedly does not clearly relate to what is shown in Figure 6. The brief description of Figure 6 has been amended to further clarify what is depicted in the figure. Support for the amendment is found in the specification at, for example, Figure 6. The objection has been obviated, and Applicants respectfully request withdrawal thereof.

With particular reference to Figure 6, the figure shows the nucleotide sequence of a splice variant of the conserved human, murine, *D. melanogaster*, and *C. elegans nit1* cDNA. Nucleotides 79 to 109 are not present in an alternatively spliced variant of the sequence shown. In the splice variant not shown, in which nucleotides 79 to 109 are not present, the ATG start codon spans nucleotides 77, 78, and 110 of the sequence shown and, consequently, the first amino acid of the encoded polypeptide, which is amino acid residue 37 shown in Figure 6, is a lysine residue encoded by nucleotides 111-113. The final amino acid of the polypeptide encoded by the alternatively spliced variant is encoded by nucleotides 1084-1086

of the sequence shown in Figure 6 and is amino acid residue 362. Amino acid residues 37 to 362 shown in Figure 6, which are encoded by the alternate splice variant not shown, correspond to residues 2 to 327 of the amino acid sequence shown in SEQ ID NO:21.

The amino acid sequence of SEQ ID NO:25 is the amino acid sequence deduced from nucleotides 1 to 1086 of the *nit1* cDNA sequence shown in Figure 6 (SEQ ID NO:1).

II. New Matter

Claims 1 to 3, 10, and 11 have been rejected under 35 U.S.C. § 112, first paragraph as being based upon a specification into which new matter has allegedly been introduced. Without conceding the correctness of the rejection, and to advance prosecution, the alleged new matter has been deleted from the specification, as previously discussed. The rejection has been obviated, and Applicants respectfully request withdrawal thereof.

III. Alleged Lack of Enablement

Claims 1 to 3, 10, and 11 have been rejected under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. Applicants respectfully traverse the rejection because it appears to be directed to the cancelled method claims.

"The enablement requirement refers to the requirement of 35 U.S.C. § 112, first paragraph that the specification describe how to make and how to use the invention. The invention that one skilled in the art must be enabled to make and use is that ***defined by the claim(s) of the particular application or patent.***" M.P.E.P. § 2164 (emphasis added).

Applicants respectfully request reconsideration and withdrawal of the rejection as it appears to be directed to the cancelled method claims. Applicants are only required to enable

that which is ***claimed in the application***. Claims 1 to 3 and 10 to 12 did not recite methods of treatment, nor do present claims 17 to 24.

The Office Action asserts the following:

> The specification does not contain any guidance whatsoever as to how the claimed invention should be used either to treat or to diagnose any disease, nor does it even disclose what disease(s) could be treated or diagnosed. There are no working examples of using the claimed invention for either treatment or diagnosis. There is no evidence presented in the specification that a change in NIT1 function or expression is related to any disease. Consequently, it is completely unpredictable what disease(s), if any, the invention could be used to treat or diagnose.

(Office Action issued May 9, 2002, page 6). In addition, with respect to the enablement rejection, the Office Action refers to the "lack of guidance or working examples which demonstrate or correlate to any therapeutic effect of the ***claimed methods***" and also refers to "the claims ***directed to a method of treating or preventing any disease or disorder*** in any subject..." (Office Action issued May 9, 2002, page 10)(emphasis added). Accordingly, the rejection appears to be based on cancelled claims 13, 14, and 16, which were directed to methods for treating or preventing a disease or disorder. Present claims 17 to 24 do not recite methods of treating or preventing a disease or disorder, nor did claims 1 to 3, 10 and 11. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection because the specification enables those of skill in the art to make and use the full scope of the subject matter *defined by the present claims*.

IV. Alleged Lack of Written Description

Claims 1 to 3 and 10 have been rejected under 35 U.S.C. § 112, first paragraph for lack of written description because the specification allegedly fails to describe a genus of

"NIT1 genes" or a genus of nucleic acids encoding a "Nit1 protein". Without conceding the correctness of the rejection, claims 1 to 3 and 10 have been cancelled, rendering the rejection moot. In addition, new claims 17 to 24 do not recite "NIT1 genes" or "Nit1 proteins". Accordingly, Applicants respectfully request withdrawal of the rejection.

V. Alleged Indefiniteness

Claims 1 to 3, 10 and 11 have been rejected under 35 U.S.C. § 112, second paragraph as indefinite because it is allegedly unclear what is encompassed by the phrase "NIT1 gene." Without conceding the correctness of the rejection, claims 1 to 3, 10 and 11 have been cancelled, rendering the rejection moot. In addition, new claims 17 to 24 do not contain the phrase "NIT1 gene." Accordingly, Applicants respectfully request withdrawal of the rejection.

VI. Alleged Anticipation

Claims 1 and 10 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Hillebrand, *et al.*, *Gene* 170(2):197-200 (1996) (hereinafter "the Hillebrand reference). Claims 1 and 10 have been cancelled, rendering the rejection moot. In addition, the Hillebrand reference fails to disclose or suggest every element of new claims 17 to 24, and, therefore, fails to anticipate claims 17 to 24.

The Hillebrand reference describes the *Arabidopsis thaliana nit1* gene, which encodes the *Arabidopsis thaliana* NIT1 protein. The Hillebrand reference fails to disclose or suggest an isolated DNA molecule comprising a DNA sequence that encodes a ***human*** NIT1 protein, or a fragment thereof having at least 10 nucleotides, as recited in new claim 17. Moreover, the Hillebrand reference fails to disclose or suggest a DNA molecule comprising a nucleotide

sequence complementary to at least 10 nucleotides of ***SEQ ID NO:1***, as recited in new claim 21. The Hillebrand reference, therefore, fails to anticipate the present claims, and Applicants respectfully request withdrawal of the rejection.

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. Accordingly, an early and favorable Action is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,

Jane Inglese

Date: November 5, 2002

Jane E. Inglese, Ph.D.
Registration No. **48,444**

WOODCOCK WASHBURN LLP
One Liberty Place - 46th Floor
Philadelphia, PA 19103
(215) 568-3100

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph beginning at line 4 of page 6 of the specification and ending at line 5 of page 6 has been amended as follows.

Fig. 6. A splice variant of the highly [Highly] conserved [sequence of] human, murine, *D. melanogaster*, and *C. elegans* [NIT1] *nit1* cDNA sequence [gene] (SEQ ID NO:1) [and protein] and the polypeptides and peptides deduced from the nucleotide sequence (SEQ ID NO:25 [thru] through SEQ ID NO:31).

The paragraph beginning at line 12 on page 6 of the specification and ending at line 6 on page 7 has been amended as follows.

One million plaques of a mouse genomic library (bacteriophage library from strain SVJ129, Stratagene, La Jolla, CS) and one hundred thousand plaques of a *D. melanogaster* genomic library were screened with corresponding cDNA probes. Clones were purified and DNA was isolated. Sequencing was carried out using Perkin Elmer thermal cyclers and ABI 377 automated DNA sequencers. DNA pools from a human BAC library (Research Genetics, Huntsville, AL) were screened by PCR with *NITI* primers (TCTGAAACTGCAGTCTGACCTCA (SEQ ID NO:2) and CAGGCACAGCTCCCCTCACTT (SEQ ID NO:3)) according to the supplier's protocol. The DNA from the positive clone, 31K11, has been isolated using standard procedures and sequenced. Chromosomal localization of the human *NITI* gene was determined using a radiation hybrid mapping panel (Research Genetics) according to the supplier's protocol and with the same primers as above. To map murine *Nitl* gene, Southern blot analysis of genomic

DNA from progeny of a (*AEJ/Gn-a bp^H/a bp^H x M. spretus)*F1 x *AEJ/Gn-a bp^h/a bp^h* backcross was performed using a full length murine *Nitl* cDNA probe. This probe detected a unique 2.0 kb DraI fragment in AEJ DNA and a unique 0.75 kb fragment in *M. spretus* DNA. Segregation of these fragments were followed in 180 N2 offspring of the backcross. Additional Mit markers (*D1Mit34, DIMit35*, and *DIMit209*) were typed from DNA of 92 mice by using PCR consisting of an initial denaturation of 4 minutes at 94°C followed by 40 cycles of 94°C for 30 seconds, 55°C for 30 seconds and 72°C for 30 seconds. Linkage analysis was performed using the computer program SPRETUS MADNESS: PART DEUX. Human and mouse*NITI* expressed sequence tag (EST) clones were purchased from Research Genetics. The sequences of human and murine *NITI* genes and cDNAs and *D. melanogaster* and *C. elegans Nit-Fhit* cDNAs have been deposited in GenBank [(accession nos. AF069984-AF069989)].

The paragraph beginning at line 1 of page 13 of the specification and ending at line 6 of page 13 has been amended as follows.

A radiation hybrid mapping panel (GeneBridge 4) was used to determine the chromosomal localization of the human *NITI* gene. By analysis of PCR data at the Whitehead/MIT database [(http://www.genome.wi.mit.edu)] on the world wide web at genome.wi.mot.edu, the *NITI* gene was localized 6.94 cR from the marker CHLC.GATA43A04, which is located at lq21-lq22.

In the Claims:

Claims 1 to 3 and 10 to 12 have been cancelled.

New claims 17 to 24 have been added.